

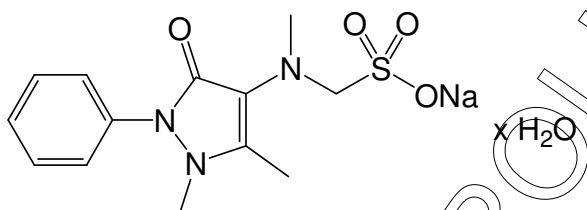
# Certificate of Analysis

**LGC Quality**

**ISO Guide 34:2009**  
DAkkS D-RM-14176-01-00  
**ISO/IEC 17025:2005**  
DAkkS D-PL-14176-01-00  
**ISO 9001:2008**  
DQS 102448 QM08

## Primary Reference Standard

Metamizole Sodium Monohydrate



Molecular Formula:  $C_{13}H_{16}N_3NaO_4S \cdot H_2O$   
Molecular Weight: 351.36  
CAS Number: [5907-38-0]

Catalogue Number: LGCQUANT0052.00

Lot Number: 28532

Long-term Storage: 15 to 25 °C, dark

Appearance: white solid

Melting Point: 210 °C (dec.)

Assay<sup>1</sup> 'as is': 99.9 %

Uncertainty<sup>2</sup> U: 0.4 %

Date of shipment: **2016-October-04**

This certificate is valid for one year from the date of shipment provided the substance is stored under the recommended conditions.

<sup>1</sup> The value is based on the results of analytical techniques. Calibration and verification were carried out with standards traceable to SI-units. The value is expressed on an "as is" basis. The identity is verified by data from international scientific literature.

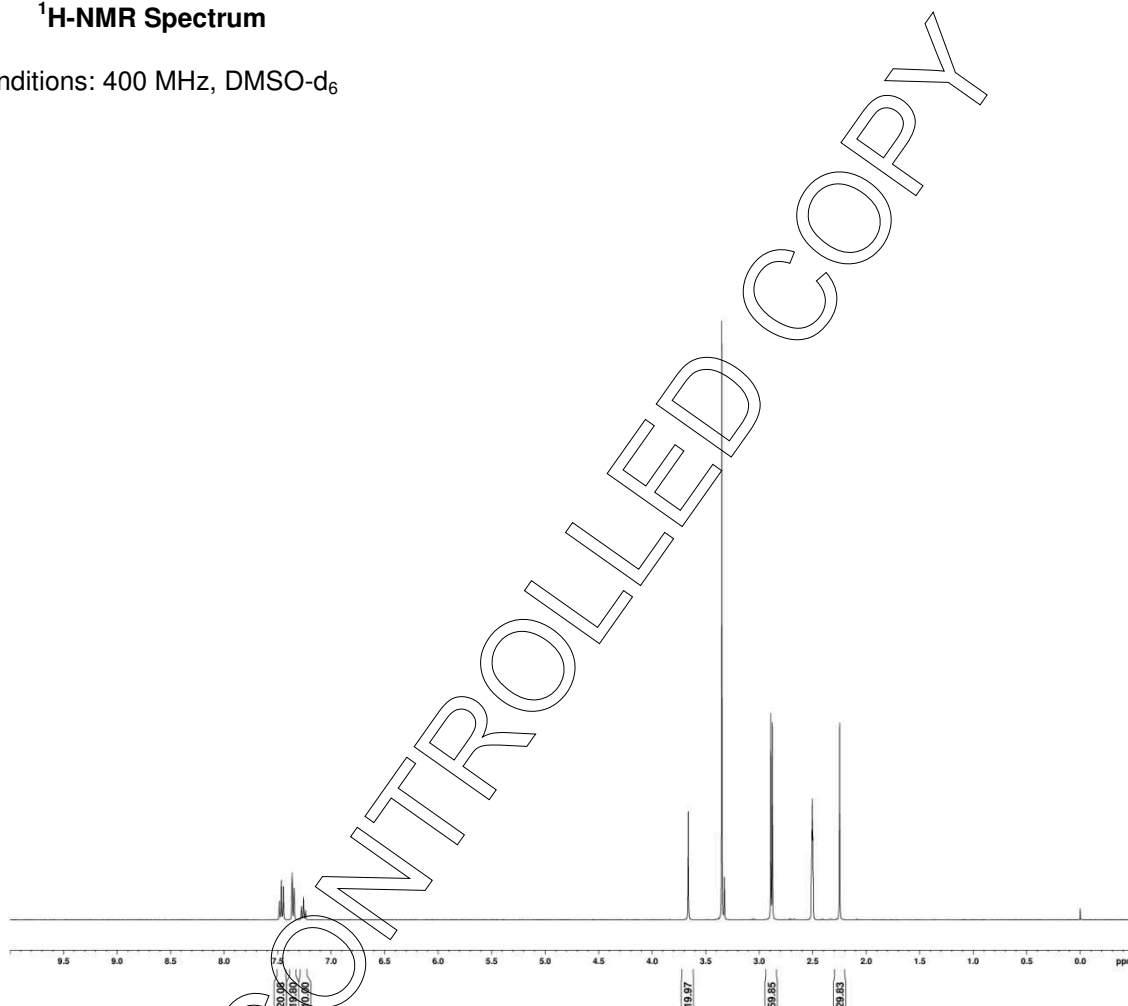
<sup>2</sup> The uncertainty "U" is the expanded uncertainty estimated in accordance with the Guide to the Expression of Uncertainty in Measurement (GUM). It is corresponding to a level of confidence of about 95 %. Coverage factor  $k = 2$ .

## I. Identity

The identity of the reference material was established by following analyses.

### 1a. <sup>1</sup>H-NMR Spectrum

Conditions: 400 MHz, DMSO-d<sub>6</sub>

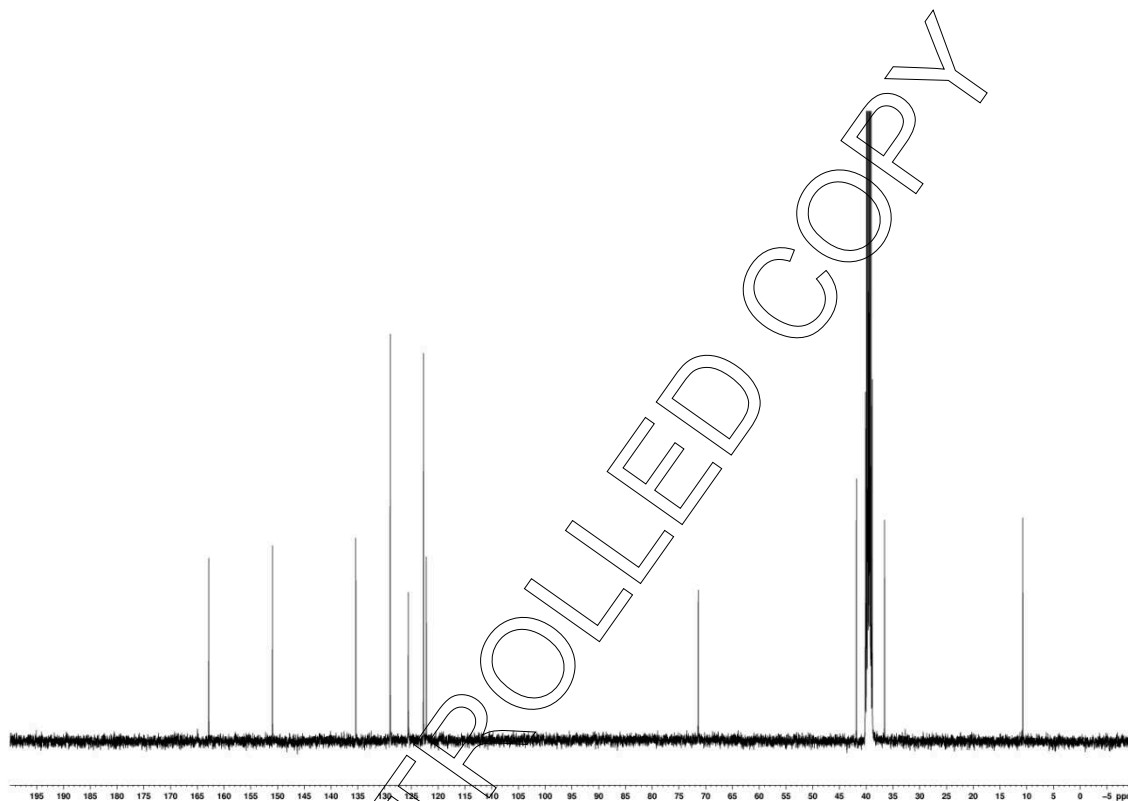


The structure is confirmed by the signals of the spectrum and their interpretation.

The signals of the NMR spectrum and their interpretation are consistent with the spectrum of EP reference substance Metamizole Sodium CRS – EP-Standard, M0600900, Batch 3.1, Id00HX03.

**Ib.  $^{13}\text{C}$ -NMR Spectrum**

Conditions: 100 MHz,  $\text{DMSO-d}_6$

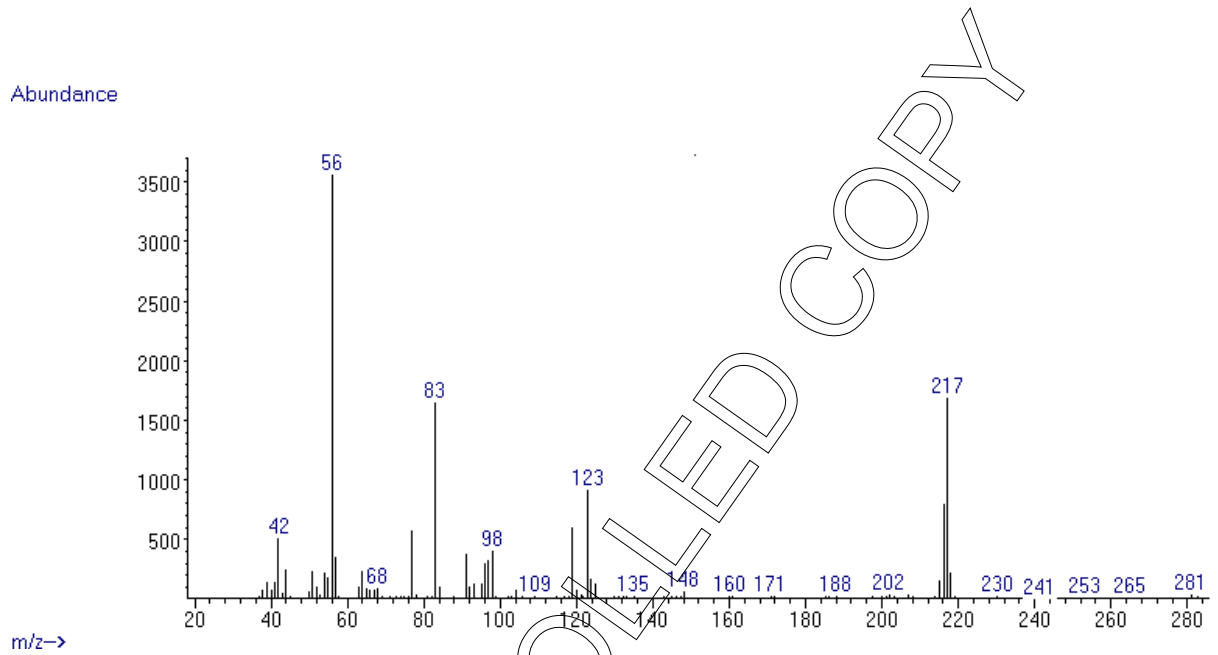


The structure is confirmed by the signals of the spectrum and their interpretation.

The signals of the NMR spectrum and their interpretation are consistent with the spectrum of EP reference substance Metamizole Sodium CRS – EP-Standard, M0600900, Batch 3.1, Id00HX03.

### Ic. Mass Spectrum

Method: EI, 70eV, detector temperature: 280 °C

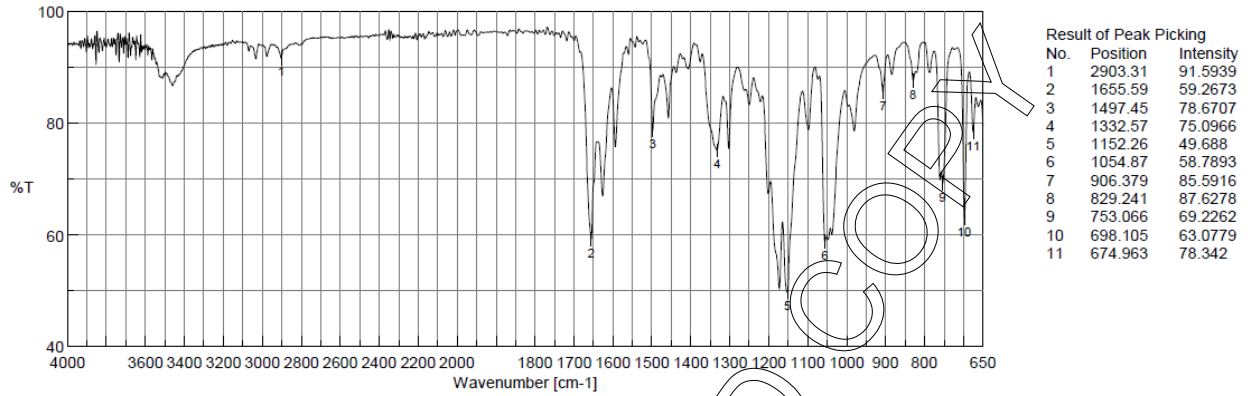


The signals of the MS spectrum and their interpretation are consistent with the structural formula.

The signals of the MS spectrum and their interpretation are consistent with the spectrum of EP reference substance Metamizole Sodium CRS – EP-Standard, M0600900, Batch 3.1, Id00HX03.

## Id. IR Spectrum

Method: Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) Spectroscopy



The signals of the IR spectrum and their interpretation are consistent with scientific literature.

The signals of the IR spectrum and their interpretation are consistent with the spectrum of EP reference substance Metamizole Sodium CRS – EP-Standard, M0600900, Batch 3.1, Id00HX03.

## le. Melting Point

Method: Capillary Method

Arithmetic mean (n=3): 210 °C (dec.)

## II. Purity

The purity of the reference material was determined by high performance liquid chromatography (HPLC).

### HPLC Conditions:

#### Column:

Luna C 18(2)  
5  $\mu\text{m}$ , 250 x 4.6 mm

#### Conditions:

1.0 ml/min, 40  $^{\circ}\text{C}$

mob. phase A: 6 g/l  $\text{NaH}_2\text{PO}_4$  + 1 ml  $\text{NEt}_3$ ,  
pH 7.0

mob. phase B: Methanol

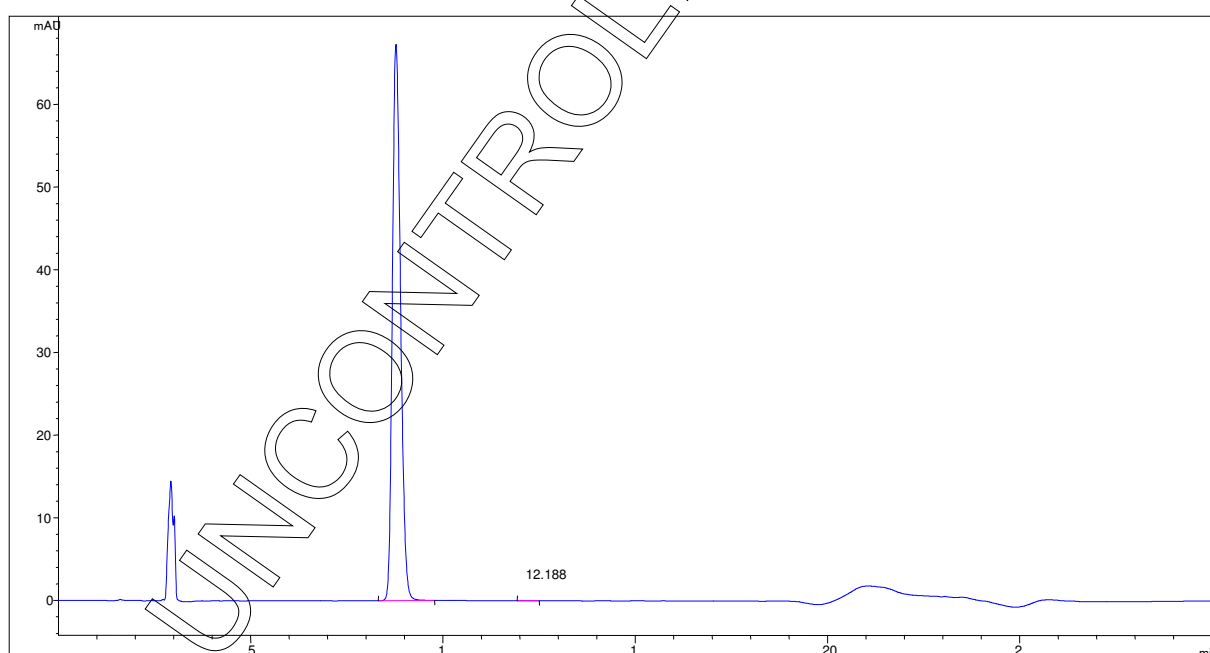
0-16 min	A/B		70/30
16-18 min	A/B	to	40/60
18-20 min	A/B		40/60
20-22 min	A/B	to	70/30
22-30 min	A/B		70/30 (v/v)

#### Detector:

DAD  
254 nm

#### Injector:

Auto  
5  $\mu\text{l}$ ; 0.25952 mg/ml in  
Dimethyl sulfoxide



### Area Percent Report - Sorted by Signal

Pk #	Retention Time	Area	Area %
1	8.78	9940.68	99.96
2	12.19	3.69	0.04
Totals		9944.37	100.00

For the calculation the system peaks were ignored. The content of the analyte was determined as the ratio of the peak area of the analyte and the cumulative areas of the purities, added up to 100 %.

#### Results:

**Average** 99.96 %  
**Number of results** n=6  
**Standard deviation** < 0.01 %

### III. Loss on Drying

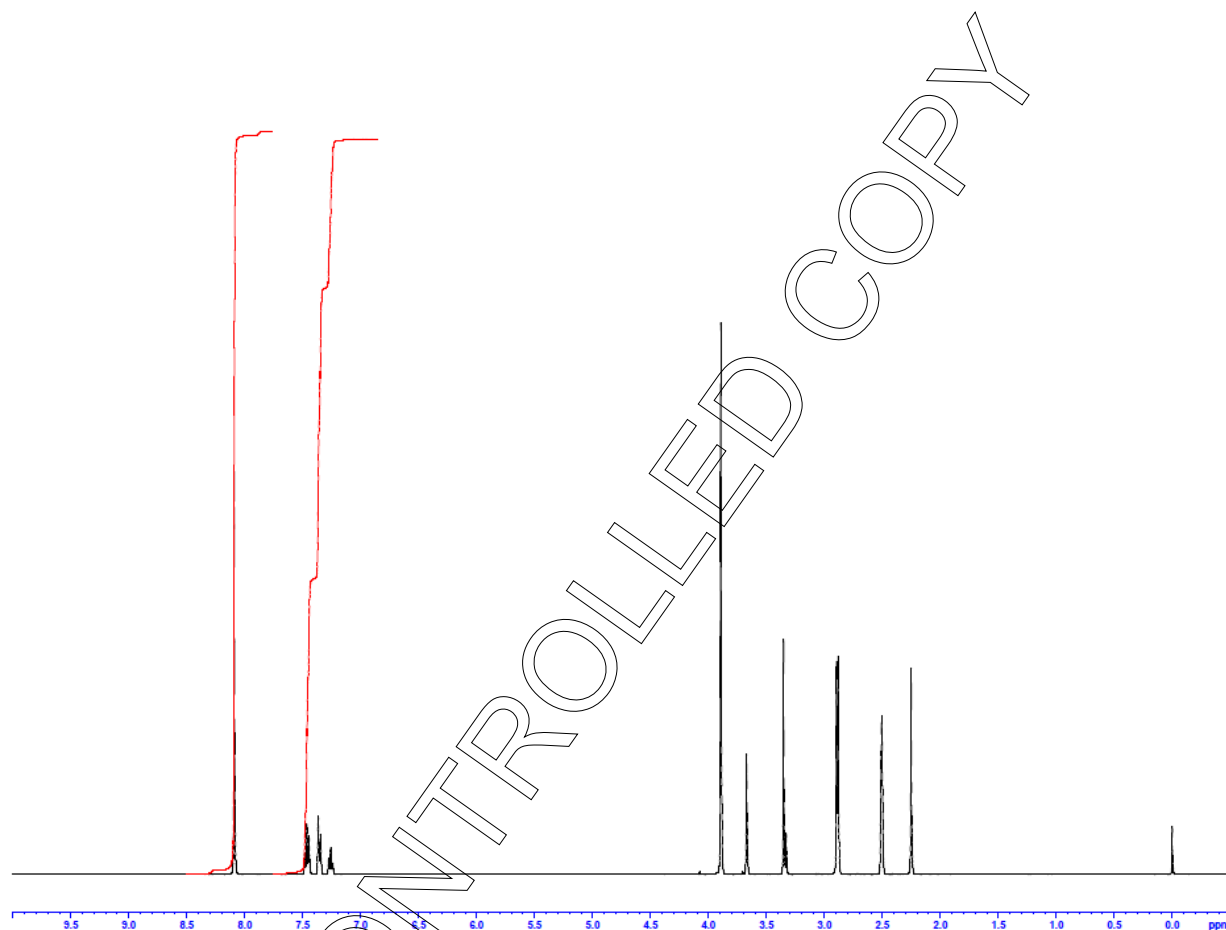
Conditions: 105 °C for 4 h, EP 7.7 (2.2.32)

#### Results:

**Average** 4.96 %  
**Number of results** n=3  
**Theoretical value** 5.13 %  
**Content of excessive water** - 0.17 %  
**Standard deviation** 0.01 %

#### IV. Assay by quantitative NMR spectroscopy

The assay of the reference substance was established by quantitative NMR spectroscopy using DMSO-d<sub>6</sub> as the solvent and with Dimethyl terephthalate (certified reference material, signal 7.76 – 8.50 ppm, 4 H) as internal standard.



#### Results:

Average	99.88 %
Number of results	n=6
Uncertainty U (expanded)	0.44 %



## V. Final Result

**Chromatographic purity (HPLC)** 99.96 %  
**Loss on drying** - 0.17 %

### Assay:

**Quantitative NMR spectroscopy** 99.88 %

The assay is assessed to be 99.9 % 'as is'

The assay 'as is' is equivalent to the assay based on the not anhydrous and not dried substance respectively. It is determined by quantitative NMR spectroscopy and its expanded uncertainty ( $k = 2$ ) is 0.4 %.

The assay is verified by the 100 % method (HPLC): 100.1 % which is inside the expanded uncertainty of the assay by quantitative NMR spectroscopy.

## VI. Stability and Homogeneity

Accelerated stability studies indicate no significant instability. The given validity period is based on this data. This is backed up by additional stability testing and historical data over the range of several years. Homogeneity assured by qualified process of preparation, verified by homogeneity testing.

Due to the homogeneity studies the minimum amount of sample to be used is 10 mg.

## VII. Further Information

### General

For laboratory use only. Not suitable for human or animal consumption.

This material conforms to the characteristics of a primary standard as described within ISO Guide 30 (Terms and definitions used in connection with reference materials).

The values quoted in this certificate are LGC's best estimate of the true values within the stated uncertainties and based on the techniques described in this certificate.



The production of this reference material was realized taking into account the principles of ISO Guide 34.

### Intended Use

Use for identification and quantification.

### Handling of the RM

Before usage of the reference material, it should be allowed to warm to room temperature.

### Assay and uncertainty

The identity and the assay are assessed by an ISO/IEC 17025 accredited testing method.

The calculation of the 100 % method (HPLC) follows the formula:

$$\text{Assay (\%)} = (100 \% - \text{LOD}) * \frac{\text{Purity HPLC (\%)}}{100 \%}$$

Volatile contents are considered as absolute contributions, HPLC purity is considered as relative contribution.

Uncertainty of the assay is expressed as an expanded uncertainty in accordance with ISO/IEC 17025 at the about 95 % level of confidence.

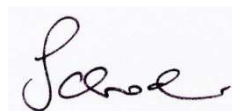
For quantitative applications use the assay as a calculation value on the as is basis. The uncertainty of the assay can be used for estimation/calculation of your own measurement uncertainty.

### Quality Control Assessment

The product quality is controlled by regularly performed quality control tests (retests).

Release Date: 2013-07-16

LGC GmbH



Dr. Sabine Schröder

Product Release



Excellence through measurement

Revision	Date	Reason for Revision
00	2013-07-16	Release of the Lot – initial version
01	2013-10-29	Accreditation Number added
02	2016-04-13	Chapter III “Loss on Drying” and result of the 100 % method in chapter V corrected
03	2016-09-13	Chapter I. Identity: phrasing modified

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